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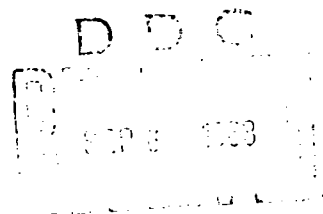
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A HUMAN GROUP ILLNESS BY INHALATION OF
THE VIRUS OF ATYPICAL FOWL PALGUE

Werner Verrerlein
8 April, 1965

A HUMAN GROUP ILLNESS BY INHALATION OF THE VIRUS OF ATYPICAL FOWL PLAGUE

Following is the translation of an article by Werner Vetterlein, published in Forschungsanstalt für Tierseuchen Insel Reims- Friedrich Loeffler Institute, Deutsche Gesundheitswesen 10(40): 1327-30, 1955. Translated by B. MacDonald.

The possibility of an infection of humans with fowl plague has been acknowledged since 1943 (Burnet[17]). Since the virus of the atypical fowl plague (Newcastle disease) has been detected in about 35 cases of diseased people, as a rule in the conjunctival rinsing fluid, but also in the inferior maxilla rinsing water, nasal secretion, blood and once in the urine (Siegert, Hausmann and Mannweiler[13]). They were even advised about small epidemics at one time with the cooking personnel (Yatom[17]) at another time by a worker in a fowl slaughterhouse. (Nelson and others [8]).

In most cases the infection in the case of people appeared unilateral, in 5 to 14 days fading conjunctivitis appeared without participation of the cornea. It is therapy resistant. Sometimes the pre-auricular lymph glands swelled. Less frequently it comes close to a slight headache and indisposition. An accurate description of that kind of infection recently expressed by Schoop [12] and Siegert, Hausmann and Mannweiler

. Finally in their last detailed work mentioned on the Newcastle (ND) infection in humans, different authors also observed a participation of the respiratory tract. Influenza like aspect of the disease and even an atypical viruspneumonia. Howitt, Bishop and Kessling (3) advised about 2 small epidemics in the states of Alabama and Tennessee. In the case of children it appeared during a light short lasting meningo-encephalitis with fever, headache and exhaustion, in the case of adults it appeared more as an influenza infection with catarrh of the upper respiratory tract. In the case of a number of patients, neutralized antibodies against the fowl plague were detected. Since one still had no knowledge then (1948) of the exceptional similarity of the antibodies in mumps and atypical fowl plague, the results can be considered individually as not completely certain. However, in the regard that the serum neutralized all 20 tests of N.D. virus, while 116 human control sera without disease symptoms did nothing, perhaps it can be concluded on the specificity of the reaction. The serological relation between mumps and N.D. compiled by Jungherr, Luginbuhl and Kilham (5,7) as well as Wenner, Jenson and Monley (15,16) especially in detail.

Specific Observations

12 to 24 hours after production of fowl vaccine from a large amount arrested all 4 laboratory technicians herewith

employed inoculating fowl embryos with Dresden strain suddenly became ill. An additional technician who had stopped temporarily in the work capacity concerned remained health. The production of vaccine took place on July 30, 1954. The diseased took a specific course as follows:

Patient L.: On 7/31/54 headache appeared about 2 o'clock, about 5 o'clock chilling. About 10 o'clock temperature rose to 38.2°. Headache, eye pressure, stiffness of throat and dorsum. The pain forced the patient to lie down flat. About 7 o'clock pain improved.

On 8/1/54 temperature between 37.8° and 38.5°. The stiffness of the throat and dorsum had disappeared, the rest of the pain had improved. Anorexia.

On 8/2/54 fever free, still moderate headache. About noon blisters the size of a pin head sprout on both corners of the mouth, and on the upper lip. Burning on the palate.

On 8/3/54 numerous very small blisters on the palate. Inflammation of the gums. Mucous membrane of the mouth very sensitive to pain and reddened. Reddening of the throat, no stench ex cre. Still slight general disease sensation.

On 8/7/54 Blisters in the mounth are swollen. Slight pain while eating.

On 8/8/54 Still moderate swelling of the gums. Ablebodied.

Patient D.: On 7/31/54 about 10 o'clock chilling and severe nausea, soon after, headache. In the evening fever of 39.6°C.

On 8/1/54 considerable headache and lumbago. No conjunctivitis, no pharyngitis. In the evening 38.3°.

On 8/2/54 pain remarkable improved but not headache.

On 8/3/54 ablebodied.

Patient M.: On 7/31/54 about 10 o'clock P.M. headache and loss of appetite beginning. Temperature was about 38°C. Increasingly severe frontal and temporal headache and pressure on the eyes. Pain in the case of optical motion. No conjunctivitis. Nausea, evening temperature 38.6°C.

On 8/1/54 no fever. Pain remarkably improved.

On 8/2/54 general feeling of weakness, besides above observation.

On 8/3/54 ablebodied.

Patient T.: On 7/30/54 light headache in the evening.

On 7/31/54 headache at forenoon then chilling and discomfort.

On 8/1/54 violent headache, loss of appetite, exhaustion, fever 39.9°C.

On 8/2/54 pain improved, subfebrile temperature.

On 8/3/54 aside from exhaustion no pain.

On 8/9/54 able-bodied.

It therefore appears that meningitic-encephalitic phenomena with severe headache, neck ache, lumbago, pressure on the eyes and eye motion, nausea, fever between 38.5° and 39.9°C also appear at the same time in all 4 patients. Conjunctivitis did not exist. Just as pharyngitis could not be proved. The herpes labialis and stomatitis aphthosa which in the case of the fading away of the primary disease dominates patient L, can belong to the frequent herpes eruption after feverish illness especially of ZNS. The patients were able-bodied at the latest 10 days afterwards. The acute manifestations faded in 2 to 3 days. Injury did not occur.

Since the suspicion of a virus disease emerged one day after the acute phase and moreover no other manifestation of an infection with fowl plague was established, a virus isolation was not tested. On re-examination of our suspicions of fowl plague infection the increase of neutralizing hemagglutination arresting antibodies in the patients was continued. The tests were carried out on only 3 diseased people since the 4th changed his address shortly after the infection, so that the second serum test for comparison failed. A serum test for each on the 5th day p.i. and about 4 weeks p.i. were withdrawn..

After Wenner, Jenson and Monley (15,16) found in the serum of people and rhesus monkeys an unspecific substance which checked the hemagglutination of fowl erythrocytes in fowl plague virus and also worked complement fixation. The titer of this unspecific hemafactor can in most favorable cases rise fourfold. The neutralizing antibodies which contain the sera of mumps convalescence frequently compared to fowl plague virus, are destroyed to a great extent according to Kelham, Jungherr and Leginbuhl (7) by heating the serums to 60° for 20 minutes.

Proof of hemagglutination arresting antibodies in the serum of patients

Egg fluid 10 to 12 days old of chicken embryos were used as antigens, which were inoculated with the homologous strain "Dresden" of atypical fowl plague virus. The infected egg fluid had a minimal titer of 10^{-7} . For the hemagglutination arresting test a titer of 10^{-6} was used. 0.5 ccm of free flowing dilution of patient serum to the second power was used. 0.5 ccm of virus dilution and 1.0 ccm of a 1% fowl erythrocyte suspension were combined in a testtube. After 75 minutes the results were gathered. Especially clear were the increases of hemagglutination arresting antibodies in the serum of Patient D. These serums arrested 5 days p.i. only undiluted and after 4 weeks in a dilution of 2^{-4} . The 2 other sera showed only a titer of 1: to 2 powers.

Results of neutralizing antibodies in patient serums

Because of the similarity of mumps antibodies with those of NDV the patients in the anamase were questioned especially after having mumps. Only patient D had had mumps 15 years before. The serums were withdrawn from the sick 5 days p.i. (serum 1) and 4 weeks p.i. (serum 2) and for the time being heated for 20 minutes at 60° , in order to disturb, possibly to do away with unspecific antibodies.

Next the dilution with isotonic sodium chloride solution in arithmetic progressions of 4^{-1} to 4^{-4} followed. The strain "Dresden" with an MID of 10^{-7} served as antigen. Nine parts diluted patient serum were given to 1 part virus dilution, amounted to 10^{-5} and 10^{-6} . By it 2 neutralization series were prepared (Table 2a and 2b) under testing of Serums 1 and 2 of each patient occasional in the same test. The neutralization mixture stood an hour at room temperature. They obtained from them 10 daily inoculated fowl egg each 0.2ccm applied in the allantoid sack. Virus and serum controls were prepared. In the case of a working titer of 10^{-5} (MID 10^{-7}) the neutralizing serum titer rose in the case of 2 patients within 4 weeks from 1:4 to 1:16. In the case of patient L the titer was at the beginning under 1:4 and then likewise rose to 1:16. In the case of a virus concentration of 10^{-8} there existed in the case of patients L and M on the 5th day of sickness a neutralizing serum titer of 1:64. After 4 weeks patient L showed no distinct titer rise, although the time of death of the egg in a solution of 1:256 was somewhat prolonged. In the case of patient M the titer rose from 1:64 to 1:256 while in the case of patient D serum 1 detected 1:4 and serum 2 in 1:64 neutralized ND virus. In the case of patients M and D the serum titer rose in both test series fourfold. The neutralizing antibodies contain the smallest requirement for reproduction, which permits a diagnosis. (Siegert, Hausmann and Mannweiler (13)).

Seven months later in the serum of the patients no more

antibodies were detected with the atypical fowl strain "Dresden".

Discussion

The detection of a fowl plague infection by serological methods is frequently unsatisfactory because of disturbing un-specific antibodies. We have nevertheless undertaken it in the case of sudden appearance of group diseases with individual symptomatology, which appeared after production of a large amount of fowl plague vaccine. The disease occurs in the form of a volatized feverish meningo-encephalitis, since they have also been described by Howitt, Bishop and Kessling (3). Since this influenza like disease was recorded during the observation time of the staff management, this impressive group disease perplexes us. Although one of the patients (M) already had produced before fowl plague vaccine, without being sick, still in this case the mechanical separation of vaccine was different from the preceeding tests and was used the first time for the fowl plague vaccine. The arrested fowl embryos have been homogenized in a high speed grinder. In this case the possibility consists in reducing to dust the processed raw materials from the filler neck in the air of the work room. Moreover, the latter used grinder was possible also from the vent pipe. Finally the disease declared that they had deflected while decanting the vaccine into a large flask of dark glass often thick over the flasck opening, in order to control the filling of the flask. In the room there was a distinct odor of treated materials and their admixture. The infectious mass was not touched by the hand. The possibility of an airborne infection was deduced from conditions. Infected animals were also grown in the air. One has applied these infectious ways in America for immunization by cooking with weakened viruses (Jungherr (4)). Many virus strains of atypical fowl plague develop especially frequently cerebral symptoms (Potel (9)). With NDV strains the protracted progress of the disease appear with cerebral disturbances. By intracerebral inoculation of Ndvirus Wenner and Lash (14) as well as Collier, Polak and Verhaart (2) obtained in rhesus monkeys an encephalitis which showed perivascular infiltration with lymphocytes and plasma cells and defficient proliferation of neuroglia cells. Collier and co-workers (2) compared the discovery with the Japanese B-encephalitis. While in most cases conjunctivitis and irrigation of the upper respiratory tract appertain to the clinical picture of the human ND virus infection and by a direct influence of stimulants on their entrance orifice can be limited, the absence of microscopically discernable stimulus of this tissue is remarkable in our patient. Perhaps the inhalation of relatively inferior virus concentrations over a period of time is appropriate, the local alteration of the mucous membranes are advanced however not enough, in order to effect on the hematogenic course a clear stimulation of the brain. Since a large group disease

Table 2

The Neutralizing Antibodies in Patient Serum.
(Virus MID 10^{-7} , Working Titer 10^{-5})

Pat. Ser.		Serum Dilution												S.X.	V.K.
		1:4	1:16		1:64		1:256								
L.	1	(24)66 66	66 66	-	48 48	48 43	43 48	---					---	43 48 48	
L.	2	---	---		66 66	73 73	73 96	---					---		
D.	1	---	43 48	73	73 73	73 43	43 48	---					---		
D.	2	---	---		96 96	96 96	96	---					---		
M.	1	---	66 66	73	73 73	96 43	48 48	---					---		
M.	2	---	- -	43	73 73	96 48	73 96	---					---		
(Working Titer 10 ⁻⁶)															
L.	1	- - 73	- - 66		- - 48	43 48	66	---					---	43 48 66	
L.	2	---	---		- -	48 66	96	---					---		
D.	1	---	- 73 73		48 48	73 48	48 66	---					---		
D.	2	---	- - 96	---		96 96	96	---					---		
M.	1	---	- 73 96	---		- 43 96	---	---					---		
M.	2	--(24)	--(24)	---		- - 48	---	---					---		

() = Unspecific dead eggs

- = Surviving

24 thru 96 = Work time in hours.

S.K. = Serum Control

V.K. = Virus Control

Table 1

The Hemagglutination Inhibiting Antibodies in Patient Serum
(Virus MID 10^{-7} , Working Titer 10^{-6})

Patient Serum		Serum Dilution						
		Undil.	2 ⁻¹	2 ⁻²	2 ⁻³	2 ⁻⁴	2 ⁻⁵	2 ⁻⁶
L.	1	+	+	+++	+++	+++	+++	++++
L.	2	-	-	-	+	++	+++	+++
D.	1	+	+++	+++	+++	+++	+++	+++
D.	2	-	-	-	±	++	+++	+++
M.	1	-	+	++	++	+++	+++	+++
M.	2	-	-	+	+	++	+++	+++

Since a single large group illness of fowl plague-conjunctivitis has been described by Nelson and co-workers (8), Yatom (17) and Rodnot and Wallner (11), this virus infection is interesting for work protection. In the breeding of eggs and in the management, the disease picture should be noticed, the dead fowl produce. The prevention of an air infection of the eye is not difficult with the knowledge of communication. The diffusion of infectious material in the case of vaccine production should be avoided. Since an intentional reducing to dust of pretreated ND virus is not residual to the immunization by our cooking, the source of infection is eliminated.

Summary

It is noted that a group sickness of 4 laboratory technicians became ill after production of a large amount of atypical fowl plague. They proceeded under the picture of a short, feverish infected with cerebral and meningitic stimulous appearances. Permanent clinical damage remains behind. In the serum of 3 patients the increase of neutralizing antibodies in the reconvalesence was established 4 times in the case of 1 sick man the increase of hemagglutination antibodies was 6 fold. It must be assumed to be an airborne infection.

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